

larger radius curve. In other embodiments, the channel can have a rectangular cross-sectional shape and at least one dimension of the rectangular cross-sectional shape can vary from inflection point to inflection point in the sigmoidal curve.

**[0020]** In the enumerated aspects or in any of their embodiments, methods for focusing particles can include passing the moving fluid from the channel into at least two output branches wherein one of the output branches is located so as to receive the localized flux of particles enriched in first particles of a given size. Receiving the localized flux can thereby increase the concentration of first particles in solution. In some embodiments, the method can include passing the moving fluid from the channel into at least two output branches wherein one of the output branches is located so as to receive the localized flux of particles enriched in first particles of a given size. A detector can be applied to enumerate particles traveling in the localized flux of particles in the channel. Methods can further include a tagging system for tagging selected particles with a tag that can be detected by the detector, the detector thereby detecting and enumerating the selected particles. In any and all aspects, methods can include systems in which the focusing can result exclusively from the inertial forces. Other method embodiments can include systems in which the focusing can result from inertial and other forces.

**[0021]** In any of the aspects, embodiments can include an apparatus wherein the cross sectional shape and area of the channel can be consistent from the inlet to the outlet. In other embodiments, the cross sectional shape and area of the channel can vary from the inlet to the outlet. The one or more localized stream lines can have a width that is less than or equal to about five times, four times, three times, two times, and/or 1.05 times the predetermined particle size. Moving the fluid suspension having particles of a predetermined size from the inlet to the outlet focuses the particles of a predetermined size into four localized streams, two localized streams, and/or a single localized stream.

**[0022]** In the enumerated aspects or in any of their embodiments, the apparatus can further include at least first and second outlet branches formed at an outlet portion of the channel, at least one of the first and second outlet branches being located on the substrate so as to receive the particles of a predetermined size from the single localized stream. In some embodiments, the aspect ratio of the rectangular cross-section results in the focusing of particles into two streams. Further, the focusing of particles into one or more localized stream lines can space the particles approximately evenly longitudinally. In other embodiments, the location of the focused stream depends upon inertial forces and Dean drag forces acting on the particles. The location can further depend upon centrifugal forces acting on the particles.

**[0023]** In any of the aspects, embodiments can include an apparatus wherein a cross sectional dimension of the channel varies. In some embodiments, the cross sectional dimension of the channel changes after each inflection of the curve. A plurality of channels can be provided on the substrate and can be configured to allow parallel flow. In other embodiments, a plurality of channels can be provided on the substrate, and at least some of the channels can be configured to allow serial flow. A plurality of channels can be provided on the substrate and a first channel can have first and second output branches

leading to second and third channels respectively. At least two of the channels can be configured to focus particles of different predetermined diameters.

**[0024]** In the enumerated aspects or in any of their embodiments, the system can further include a tagging system that can be a passive sorting system. The tagging system can apply to the particles to be segregated a tag having a property that can be forced out of the focused particle stream by the sorting system. The tag can increase the particle size and the sorting system can include a channel geometry that segregates particles into the first and second output branches based upon size. In some embodiments, the tag can include a magnetic property and the sorting system can include a magnetic biasing element that applies a force to the tagged particles that diverts the tagged particles from the second to the first output branch. In other embodiments, the tag can include an electric property and the sorting system can include an electrophoretic force to the tagged particles that diverts the tagged particles from the second to the first output branch. The sorting system can include an affinity column that diverts the tagged particles from the second to the first output branch.

**[0025]** In any of the aspects, embodiments can include a sorting system which is an active sorting system and can further include a controller for selectively diverting tagged particles from the second to the first output branch. The sorting system can further include a detector for detecting tagged particles, the detector being operatively connected to the controller to signal to the controller the presence of a tagged particle for diversion. The detector can be a fluorescence detector and the tags can be fluorescent tags.

**[0026]** In any of the aspects, certain embodiments of the sorting system can further include a channel resistance actuator, the channel resistance actuator being selectively actuated by the controller to divert tagged particles from the second to the first output branch. The channel resistance actuator can be coupled to the first output branch to lower the fluid resistance of the first output branch to divert a tagged particle from the second to the first output branch. In some embodiments, the channel resistance actuator can be coupled to the second output branch to increase the fluid resistance of the first output branch to divert a tagged particle from the second to the first output branch. The channel resistance actuator can be a microvalve that partially opens or closes to change the fluid resistance of an output branch. In other embodiments, the channel resistance actuator can stretch or squeeze a dimension of the channel to change the fluid resistance of an output branch. In any of the aspects, the particles can be cells and the cells can be sorted based upon a property of the cell. In some embodiments, the property of the cell for which it is sorted is the presence of at least one indicator of cancer.

**[0027]** In the enumerated aspects or in any of their embodiments, methods for separating target particles from a population of particles can be provided wherein the dividing is done passively. The target particles can have a different size than other particles in the population and the target particles can form a localized flux in a predetermined location within the channel. In some embodiments, an entrance to the first output branch can be located so as to encompass the predetermined location within the channel of the localized flux of target particles. Embodiments of the method can also include selectively tagging particles with a tag that is used by a dividing system operatively connected to the channel. The tag can increase the size of the selectively tagged particles and the tag can be a magnetic tag.